CLAIMS

What is claimed is:

1. An isolated nucleic acid encoding a fibroblast growth factor-23 (FGF23) or a mutant, variant, homolog, or fragment thereof.

2. An isolated nucleic acid encoding a fibroblast growth factor-23 (FGF23) wherein said isolated nucleic acid shares at least about 50% sequence identity with a nucleic acid sequence of at least one of SEQ ID NO:1 and SEQ ID NO:3.

3. An isolated nucleic acid encoding a fibroblast growth factor-23 (FGF23) wherein said isolated nucleic acid encodes a polypeptide having an amino acid sequence that shares at least 40% sequence identity with an amino acid sequence of at least one of SEQ ID NO:2 and SEQ ID NO:4.

4. An isolated nucleic acid included in DSMZ Deposit No. DSM 13530.

5. The isolated nucleic acid of claim 1, said isolated nucleic acid further comprising a nucleic acid encoding a tag polypeptide covalently linked thereto.

6. The isolated nucleic acid of claim 5, wherein said tag polypeptide is selected from the group consisting of a myc tag polypeptide, a glutathione-S-transferase tag polypeptide, a green fluorescent protein tag polypeptide, a myc-pyruvate kinase tag polypeptide, a His6 tag polypeptide, an influenza virus hemagglutinin tag polypeptide, a flag tag polypeptide, and a maltose binding protein tag polypeptide.

7. The isolated nucleic acid of claim 1, said nucleic acid further comprising a nucleic acid specifying a promoter/regulatory sequence operably linked thereto.

8. A vector comprising the isolated nucleic acid of claim 1.

9. The vector of claim 8, said vector further comprising a nucleic acid specifying a promoter/regulatory sequence operably linked thereto.

10. A recombinant cell comprising the isolated nucleic acid of claim 1.

11. A recombinant cell comprising the vector of claim 8.

12. An isolated nucleic acid complementary to a nucleic acid encoding a fibroblast growth factor-23 (FGF23) or a mutant, variant, homolog, or fragment thereof, said complementary nucleic acid being in an antisense orientation.

13. The isolated nucleic acid of claim 12, wherein said complementary nucleic acid shares at least 50% sequence identity with a nucleic acid complementary with a nucleic acid having the sequence of at least one of SEQ ID NO:1 and SEQ ID NO:3.

14. A vector comprising the isolated nucleic acid of claim 12.

15. The vector of claim 14, said vector further comprising a nucleic acid specifying a promoter/regulatory sequence operably linked thereto.

16. A recombinant cell comprising the isolated nucleic acid of claim 12.

17. A transgenic non-human mammal comprising an isolated nucleic acid encoding a fibroblast growth factor-23 (FGF23) or a mutant, variant, homolog, or fragment thereof.

18. An isolated polypeptide comprising a fibroblast growth factor-23 (FGF23) or a mutant, variant, homolog, or fragment thereof.

19. The isolated polypeptide of claim 18, wherein the amino acid sequence of said FGF23 shares at least about 40% sequence identity with an amino acid sequence of at least one of SEQ ID NO:2 and SEQ ID NO:4.

20. An antibody that specifically binds with a fibroblast growth factor-23 (FGF23) polypeptide, or a mutant, variant, homolog, or fragment thereof.

21. The antibody of claim 20, wherein said antibody is selected from the group consisting of a polyclonal antibody, a monoclonal antibody, a humanized antibody, a chimeric antibody, and a synthetic antibody.

22. An isolated nucleic acid encoding a fibroblast growth factor-23 (FGF23) wherein said nucleic acid comprises a mutation.

23. The isolated nucleic acid of claim 22, wherein said mutation confers increased stability on said FGF23.

24. The isolated nucleic acid of claim 22, wherein said mutation is selected from the group consisting of a mutation in the nucleic acid encoding amino acid 176 (arginine) relative to SEQ ID NO:2 and a mutation in the nucleic acid encoding amino acid 179 (arginine) relative to SEQ ID NO:2.

25. An isolated fibroblast growth factor-23 (FGF23) polypeptide, wherein said polypeptide comprises a mutation.

26. An isolated fibroblast growth factor-23 (FGF23) polypeptide, said polypeptide comprises a mutation that confers increased stability on said FGF23.

27. The isolated polypeptide of claim 26, wherein said mutation is selected from the group consisting of a mutation at amino acid 176 (arginine) relative to SEQ ID NO:2 and a mutation at amino acid 179 (arginine) relative to SEQ ID NO:2.

28. An inhibitor of fibroblast growth factor-23 (FGF23) wherein said inhibitor is selected from the group consisting of a molecule that reduces the level of mRNA encoding FGF23 polypeptide, a molecule that reduces the level of FGF23 polypeptide, and a molecule that reduces a biological activity of FGF23.

29. The inhibitor of claim 28, wherein said inhibitor is selected from the group consisting of an antisense nucleic acid, a ribozyme, an antibody, a peptide, and a peptidomimetic.

30. The inhibitor of claim 28, wherein said inhibitor is an antibody selected from the group consisting of an antibody that specifically binds with FGF23 and an antibody that specifically binds with an FGF23 receptor.

31. The inhibitor of claim 28, wherein said inhibitor is double stranded RNA that reduces the level of said mRNA encoding FGF23 polypeptide by RNA interference.

32. A composition comprising the isolated nucleic acid of claim 1 and a pharmaceutically-acceptable carrier.

33. A composition comprising the isolated nucleic acid of claim 12 and a pharmaceutically-acceptable carrier.

34. A composition comprising the isolated polypeptide of claim 18 and a pharmaceutically-acceptable carrier.

35. A composition comprising the antibody of claim 20 and a pharmaceutically-acceptable carrier.

36. A composition comprising the isolated nucleic acid of claim 22 and a pharmaceutically-acceptable carrier.

37. A composition comprising the isolated nucleic acid of claim 23 and a pharmaceutically-acceptable carrier.

38. A composition comprising the isolated nucleic acid of claim 24 and a pharmaceutically-acceptable carrier.

39. A composition comprising the isolated FGF23 polypeptide of claim 25 and a pharmaceutically-acceptable carrier.

40. A composition comprising the isolated FGF23 polypeptide of claim 26 and a pharmaceutically-acceptable carrier.

41. A composition comprising the isolated FGF23 polypeptide of claim 27 and a pharmaceutically-acceptable carrier.

42. A composition comprising the inhibitor of claim 28 and a pharmaceutically-acceptable carrier.

43. A method of making an isolated protein having the biological activity of fibroblast growth factor-23 (FGF23) comprising (a) culturing the recombinant cell of claim 11 under conditions such that said protein is expressed; and (b) recovering said protein.

44. A method of diagnosing a hypophosphatemic disorder in a mammal, said method comprising (a) obtaining a biological sample from said mammal and (b) contacting said biological sample with a reagent which detects the presence or absence of a mutation in a nucleic acid encoding fibroblast growth factor-23 (FGF23) wherein the presence of said mutation is an indication that said mammal is afflicted with said hypophosphatemic disorder, thereby diagnosing said hypophosphatemic disorder in said mammal.

45. The method of claim 44, wherein said hypophosphatemic disorder is autosomal dominant hypophosphatemic rickets (ADHR).

46. The method of claim 44, wherein said biological sample is selected from the group consisting of blood and urine.

47. The method of claim 44, wherein said reagent is a nucleic acid.

48. The method of claim 44, wherein said reagent is detectably labeled.

49. The method of claim 44, wherein said reagent is detectably labeled with a label selected from the group consisting of a radioisotope, a bioluminescent compound, a chemiluminescent compound, a fluorescent compound, a metal chelate, and an enzyme.

50. A method of diagnosing a hypophosphatemic disorder in a mammal, said method comprising (a) obtaining a biological sample from said mammal and (b) contacting said biological sample with a reagent which detects the presence or absence of a mutant form of fibroblast growth factor-23 (FGF23) polypeptide, wherein the presence of said mutant form of FGF23 polypeptide is an indication that said mammal is afflicted with said hypophosphatemic disorder, thereby diagnosing said hypophosphatemic disorder in said mammal.

51. The method of claim 50, wherein said hypophosphatemic disorder is autosomal dominant hypophosphatemic rickets (ADHR).

52. The method of claim 50, wherein said biological sample is selected from the group consisting of blood and urine.

53. The method of claim 50, wherein said reagent is an antibody.

54. A method of diagnosing a hypophosphatemic disorder in a mammal, said method comprising (a) obtaining a biological sample from said mammal and (b) contacting said biological sample with a reagent that detects the level of fibroblast growth factor-23 (FGF23) polypeptide in said sample, wherein an elevated level of FGF23 polypeptide in said sample, relative to the level of FGF23 polypeptide in a sample obtained from a control mammal, is an indication that said mammal is afflicted with said hypophosphatemic disorder, thereby diagnosing said hypophosphatemic disorder in said mammal.

55. The method of claim 54, wherein said hypophosphatemic disorder is selected from the group consisting of X-linked hereditary rickets (XLH), hereditary hypophosphatemic rickets (HHRH), hypophosphatemic bone disease (HBD), autosomal dominant hypophosphatemic rickets (ADHR), tumor induced osteomalacia, epidermal nevus syndrome, fibrous dysplasia, and nephrolithiasis.

56. The method of claim 54, wherein said biological sample is selected from the group consisting of blood and urine.

57. The method of claim 54, wherein said reagent is an FGF23 antibody.

58. The method of claim 54, wherein said reagent is detectably labeled.

59. The method of claim 54, wherein said reagent is detectably labeled with a label selected from the group consisting of a radioisotope, a bioluminescent compound, a chemiluminescent compound, a fluorescent compound, a metal chelate, and an enzyme.

60. A method of diagnosing tumor induced osteomalacia in a patient, said method comprising (a) obtaining a tumor sample from said patient and (b) detecting the expression or lack thereof of FGF23 in said tumor, wherein the expression of FGF23 is indicative that said patient has tumor induced osteomalacia.

61. A method of treating a hypophosphatemic disorder in a mammal, said method comprising administering to a mammal afflicted with said disorder a therapeutically effective amount of a fibroblast growth factor-23 (FGF23) inhibitor selected from the group consisting of an inhibitor which reduces the level of mRNA encoding FGF23 polypeptide in said mammal, an inhibitor which reduces the level of FGF23 polypeptide in said mammal, and an inhibitor of the biological activity of FGF23 in said mammal.

62. The method of claim 61, wherein said hypophosphatemic disorder is selected from the group consisting of X-linked hereditary rickets (XLH), hereditary hypophosphatemic rickets (HHRH), hypophosphatemic bone disease (HBD), autosomal

dominant hypophosphatemic rickets (ADHR), tumor induced osteomalacia, epidermal nevus syndrome, fibrous dysplasia, and nephrolithiasis.

63. The method of claim 61, wherein said inhibitor is selected from the group consisting of an antisense nucleic acid, a ribozyme, an antibody, a peptide, and a peptidomimetic.

64. A method of treating a hyperphosphatemic disorder in a mammal, said method comprising administering to a mammal afflicted with said disorder a therapeutically effective amount of an isolated nucleic acid encoding fibroblast growth factor-23 (FGF23).

65. The method of claim 64, wherein said isolated nucleic acid comprises a mutation that confers increased stability on the FGF23 polypeptide encoded thereby.

66. The method of claim 64, wherein said hyperphosphatemic disorder is selected from the group consisting of mild renal insufficiency and tumoral calcinosis.

67. A method of treating a hyperphosphatemic disorder in a mammal, said method comprising administering to a mammal afflicted with said disorder a therapeutically effective amount of an isolated fibroblast growth factor-23 (FGF23) polypeptide.

68. The method of claim 67, wherein, said isolated FGF23 polypeptide comprises a mutation that confers increased stability on said FGF23 polypeptide.

69. The method of claim 67, wherein said hyperphosphatemic disorder is selected from the group consisting of mild renal insufficiency and tumoral calcinosis.

70. A method of treating a hyperphosphatemic disorder in a mammal, said method comprising administering to said mammal afflicted with said disorder a therapeutically effective amount of a reagent that increases the level of fibroblast growth factor-23 (FGF23) polypeptide is said mammal.

71. The method of claim 70, wherein said reagent inhibits degradation of said FGF23 polypeptide.

72. The method of claim 70, wherein said hyperphosphatemic disorder is selected from the group consisting of mild renal insufficiency and tumoral calcinosis.

73. A method of treating a hyperphosphatemic disorder in a mammal, said method comprising administering to a mammal afflicted with said disorder a therapeutically effective amount of a population of cells comprising an isolated nucleic acid encoding fibroblast growth factor-23 (FGF23).

74. The method of claim 73, wherein said isolated nucleic acid comprises a mutation that confers increased stability on said FGF23 encoded thereby.

75. The method of claim 73, wherein said hypophosphatemic disorder is selected from the group consisting of mild renal insufficiency and tumoral calcinosis.

76. A method of treating osteoporosis in a mammal, said method comprising administering to said mammal a therapeutically effective amount of a fibroblast growth factor-23 (FGF23) or a reagent that increases the level of FGF23 polypeptide in said mammal.

77. A method of treating a condition involving deposition of calcium and phosphate in the arteries or soft tissues of a mammal, said method comprising administering to said mammal a therapeutically effective amount of fibroblast growth factor-23 (FGF23) or a reagent that increases the level of FGF23 polypeptide.

78. The method of claim 77, wherein said condition is dermatomyositis.

79. A method of treating coronary artery disease in a mammal, said method comprising administering to the cells of the coronary artery of an afflicted mammal a nucleic acid encoding a fibroblast growth factor-23 (FGF23).

80. A kit for diagnosing a hypophosphatemic disorder in a mammal, said kit comprising a reagent which detects the presence or absence of a mutation in the nucleic acid sequence encoding fibroblast growth factor-23 (FGF23) wherein the presence of said mutation is an indication that said mammal is afflicted with said hypophosphatemic disorder, said kit further comprising an applicator, and an instructional material for the use thereof.

81. A kit for diagnosing a hypophosphatemic disorder in a mammal, said kit comprising a reagent that detects the level of a fibroblast growth factor (FGF23) polypeptide, wherein an elevated level of said FGF23 polypeptide is an indication that said mammal is afflicted with said hypophosphatemic disorder, said kit further comprising an applicator, and an instructional material for the use thereof.

82. A kit for diagnosing a hypophosphatemic disorder in a mammal, said kit comprising a reagent which detects the presence or absence of a mutant form of a fibroblast growth factor-23 (FGF23) polypeptide, wherein the presence of said mutant form of said FGF23 is an indication that said mammal is afflicted with said hypophosphatemic disorder, said kit further comprising an applicator, and an instructional material for the use thereof.

83. The isolated nucleic acid of claim 24, wherein said mutation is selected from the group consisting of 527G>A, 535C>T and 536G>A relative to SEQ ID NO:1.